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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,349	09/01/2005	Lars R. Damgaard	HOI-13302/16	2540
25006	7590	07/15/2008	EXAMINER	
GIFFORD, KRASS, SPRINKLE, ANDERSON & CITKOWSKI, P.C			MARTIN, PAUL C	
PO BOX 7021				
TROY, MI 48007-7021			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/540,349	Applicant(s) DAMGAARD ET AL.	
	Examiner PAUL C. MARTIN	Art Unit 1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 27,36-38,40,42,43,45,48,49,51-53,57,60-67 and 70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,8,10,12,13,21,30,31,68 and 71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/27/08</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 1-3,8,10,12,13,21,27,30,31,36-38,40,42,43,45,48,49,51-53,57,60-68,70 and 71.

DETAILED ACTION

Claims 1-3, 8, 10, 12, 13, 21, 27, 30, 31, 36-38, 40, 42, 43, 45, 48, 49, 51-53, 57, 60-68, 70 and 71 are pending in this application, Claims 27, 36-38, 40, 42, 43, 45, 48, 49, 51-53, 57, 60-67 and 70 remain withdrawn **without** traverse. Claims 1-3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 were examined on their merits.

The rejection of pending Claims 1-3, 8, 10, 12, 13, 21, 30, 31 and 68 under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn due to the Applicants amendments to the claims filed 05/01/08.

The rejection of pending Claim 8 under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn due to the Applicants amendments to the claims filed 05/01/08.

The rejection of pending Claims 1-3, 8, 10, 12, 13, 21, 30, 31, and 68 under 35 U.S.C. 102(b) as being anticipated by Houghton et al (1996) has been withdrawn due to the Applicant's amendments to the claimed filed 05/01/08.

The rejection of pending Claims 1-3, 8, 10, 30, 31, and 68 under 35 U.S.C. 102(b) as being anticipated by EP 1,134,583 A1 has been withdrawn due to the Applicant's amendments to the claimed filed 05/01/08.

The rejection of pending Claims 1-3, 8, 10, 30, 31, and 68 under 35 U.S.C. 102(a) as being anticipated by Trimarchi et al (Biology of Reproduction, 2000) has been withdrawn due to the Applicant's amendments to the claimed filed 05/01/08.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 as amended requires "...allowing metabolite transport through the diffusion barrier and/or through at least one opening in the diffusion barrier..." It is unclear what purpose this addition serves as it is already stated that the diffusion barrier is capable of allowing through metabolite transport and must therefore inherently contain at least one opening otherwise the through transport could not occur. Claims 2, 3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 are rejected as being dependent upon rejected Claim 1.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "said at least one component" in lines 13-14. There is insufficient antecedent basis for this limitation in the claim. Claims 2, 3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 are rejected as being dependent upon rejected Claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 10, 13, 21, 30, 31, 68 (and extended to new claim 71) remain rejected under 35 U.S.C. 102(b) as being anticipated by Miltenberger *et al.* (US 4,649,114).

Miltenberger *et al.* teach a glass walled (gas impermeable) cylindrical device for culturing mammalian cells. They teach that this device has a diffusion barrier (membrane) made of silicone rubber or polytetrafluoroethylene that is permeable to oxygen and inherently has a viscosity greater than water (see Abstract, for example).

The barrier is in the form of a tube that is coiled around the chamber, reading on claim 2 (see col. 5 line 50 to col. 6 line 36; see Fig. 2 as examples). This chamber contains an oxygen sensor that measures the amount of oxygen being consumed by the cells in suspension, and which has the capability of adjusting oxygen input in response (see col. 6, lines 37-52, for example). This device is useful for culturing animal cells, which reads on "substantially spherical metabolizing particle" as recited in claim 1 (see reference claim 1, for example). Furthermore, Miltenberger *et al.* teach that the device can contain synthetic balls as a support for cell growth, which could read on an individual spherical metabolizing particle; however, because the claims are drawn to a device, the invention of Miltenberger *et al.* meets the instant claims limitations. Whether one of skill in the art chooses to measure one metabolizing particle or many is the user's discretion.

Claims 1-3, 8, 10, 21, 30, 31, 68 (and extended to new claim 71) remain rejected under 35 U.S.C. § 102(b) as being anticipated by Wodnicka *et al.* (2000).

Wodnicka *et al.* teach a cylindrical well microplate system comprising a luminophore in a gas-permeable silica-gel matrix (membrane) comprising an oxygen sensitive ruthenium dye; this high viscosity matrix is attached to the bottom of each gas impermeable plastic microplate well. Cells are allowed to metabolize diffused oxygen in the wells, consuming oxygen, which causes a change in the fluorescence properties of the matrix (see Materials and Methods, pp. 142-44, for example).

While the reference teaches the measurement of the metabolic rates of multiple cells, this would not preclude one from using the device to measure the metabolic rate of an individual cell based upon appropriate well size. Furthermore the instant application claims a device; regardless of intended use the device taught by Wodnicka *et al.* meets the structural limitations as instantly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 8, 10, 21, 30, 31, 68 and 71 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Miltenberger *et al.* (US 4,649,114) for reasons of record set forth in the prior action.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, 68 and 71 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Miltenberger *et al.* (US 4,649,114) in view of Schwarz *et al.* for reasons of record set forth in the prior action.

Response to Arguments

Applicant's arguments filed 05/01/08 have been fully considered but they are not persuasive.

The Applicant argues that Miltenberger *et al.* describes a device wherein the transport of metabolites is not governed by diffusion but by flow induced mixing and therefore does not disclose a device wherein a metabolite diffusion gradient is established throughout the medium in the compartment or wherein the metabolic rate of individual particles is measured non-invasively (Remarks, Pg. 15, Lines 4-13).

This is not found to be persuasive for the following reasons, Miltenberger *et al.* clearly teaches a device wherein the metabolite oxygen is diffused into the medium (see abstract for example). The measurement of the metabolic rate non-invasively of an individual particle is a functional intended use and does not materially or structurally change the claimed invention. Further, the establishment of a diffusion gradient is similarly a functional limitation of the device and does not materially change the device comprising; one compartment defined by a diffusion barrier arranged around a metabolizing particle and a detector. The MPEP states:

While features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function. *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997)

The Applicant argues that Wodnicka *et al.* does not disclose a method for evaluating the metabolic rate of individual particles, that turbulence caused by convective currents would prevent the establishment of a metabolite diffusion gradient, that the Examiner's statements regarding measurement of the metabolisms of multiple cells by the reference as applied to an embryo being an individual spherical metabolizing particle is incorrect, and that the sensitivity of the instant invention is 3 orders of magnitude better than the cited reference (Remarks, Pg. 16, Lines 2-22 and Pg. 17, Lines 1-8).

This is not found to be persuasive for the following reasons, as discussed above the establishment of a metabolite diffusion gradient is a functional limitation which does not materially change the structure of the claimed invention. Further, while the reference may teach the measurement of multiple cells this would not preclude one of ordinary skill in the art from the knowledge that adjusting well size to accommodate a single cell as opposed to upscaling for multiple cells would be a matter of personal choice. In addition, the amendment of the claim to "an substantially spherical metabolizing particle" does not preclude the analyses of a conglomeration of multiple cells as discussed in the prior action, a blastocyst or embryo would meet the limitation of the claim, giving the term its broadest, reasonable interpretation. The Applicants statements regarding the sensitivity of the claimed invention as compared to the reference cannot be evaluated lacking any evidentiary support.

The Applicant argues that the Miltenberger *et al.* reference does not establish a metabolite diffusion gradient throughout the medium (Remarks, Pg. 19, Lines 1-11).

This is not found to be persuasive for the following reasons, as discussed above the establishment of a metabolite diffusion gradient is a functional limitation which does not materially change the structure of the claimed invention. The MPEP states:

While features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function. *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997)

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (See Remarks, Pg 19, Lines 12-22 and Pg. 20, Lines 1-10), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Both references are drawn to a similar field of endeavor, which is the use of devices comprising oxygen permeable membranes in the maintenance of cell cultures.

The modification of the method of Miltenberger *et al.* to make the device further comprise an adjustable insert and/or bottom is *prima facie* obvious. The MPEP states:

In re Stevens, 212 F.2d 197, 101 USPQ 284 (CCPA 1954) (Claims were directed to a handle for a fishing rod wherein the handle has a longitudinally adjustable finger hook, and the hand grip of the handle connects with the body portion by means of a universal joint. The court held that adjustability, where needed, is not a patentable advance, and because there was an art-recognized need for adjustment in a fishing rod, the substitution of a universal joint for the single pivot of the prior art would have been obvious.).

Conclusion

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1657

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

07/09/08

/JON P WEBER/

Supervisory Patent Examiner, Art Unit 1657